

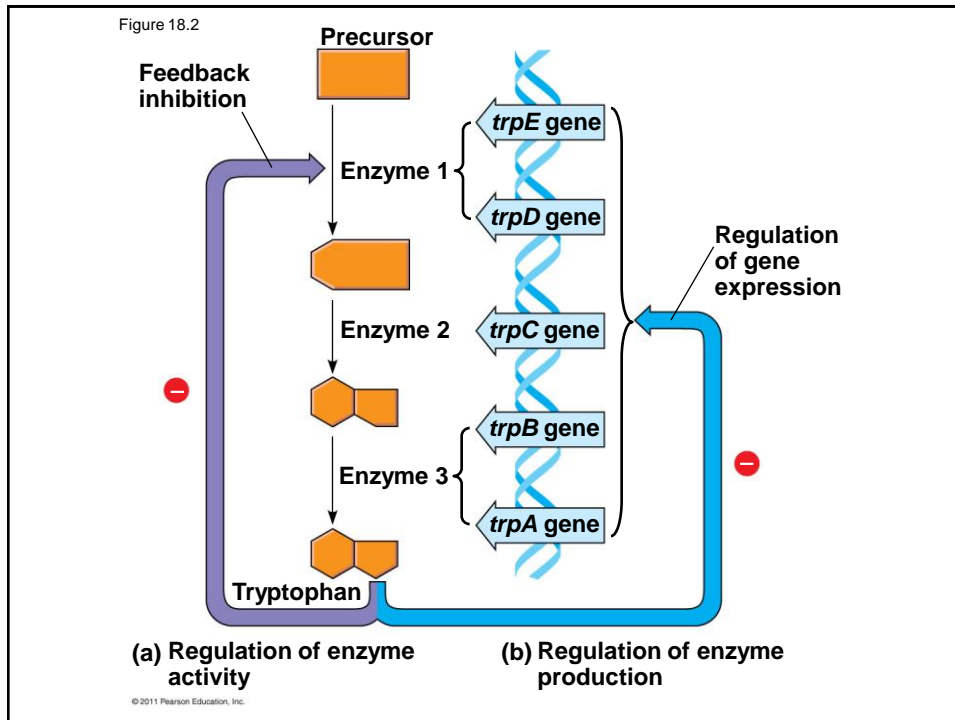
Unit 3

Part 3: Genome Regulation

AP Biology

Concept 18.1: Bacteria often respond to environmental change by regulating transcription

- Natural selection has favored bacteria that produce only the products **needed** by that cell
- A cell can regulate the production of enzymes by **feedback inhibition** or by **gene regulation**
- Gene expression in bacteria is controlled by the **operon** model



Operons: The Basic Concept

- A cluster of functionally related genes can be under coordinated control by a single “on-off switch”
- The regulatory “switch” is a segment of DNA called an **operator** usually positioned within the promoter
- An **operon** is the entire stretch of DNA that includes the operator, the promoter, and the genes that they control

- The operon can be switched off by a protein **repressor**
- The repressor **prevents** gene transcription by binding to the operator and blocking RNA polymerase
- The repressor is the product of a **separate regulatory gene**

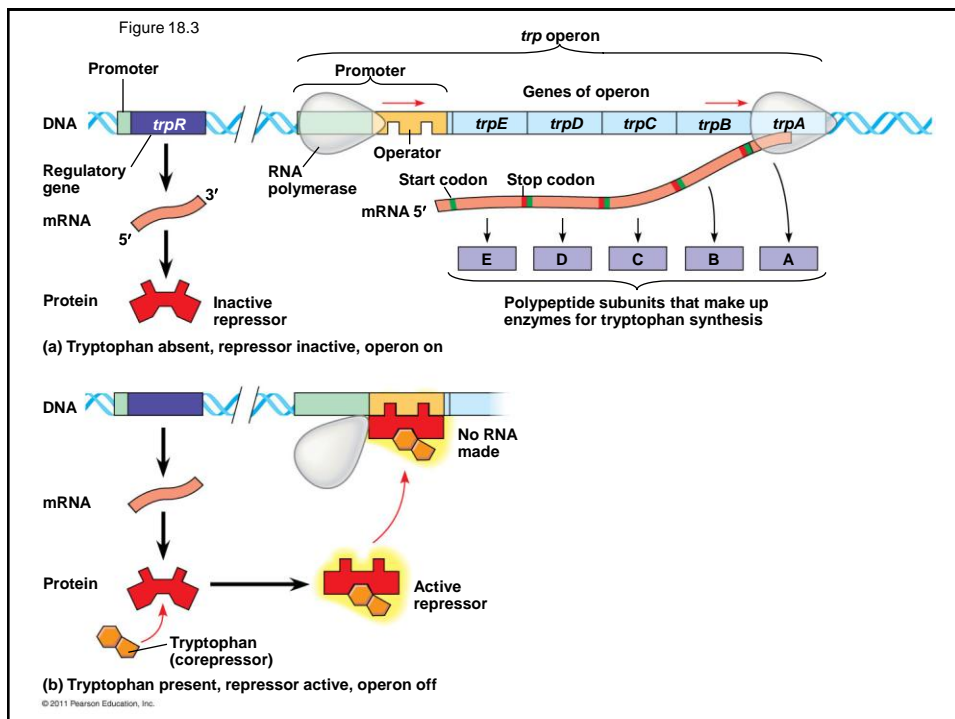
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- The repressor can be in an active or inactive form, depending on the presence of other molecules
- A **corepressor** is a molecule that cooperates with a repressor protein to switch an operon off
- For example, *E. coli* can synthesize the amino acid tryptophan

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- By default the *trp* operon is on and the genes for tryptophan synthesis are transcribed
- When tryptophan is present, it binds to the *trp* repressor protein, which turns the operon off
- The repressor is active only in the presence of its corepressor tryptophan; thus the *trp* operon is turned off (repressed) if tryptophan levels are high

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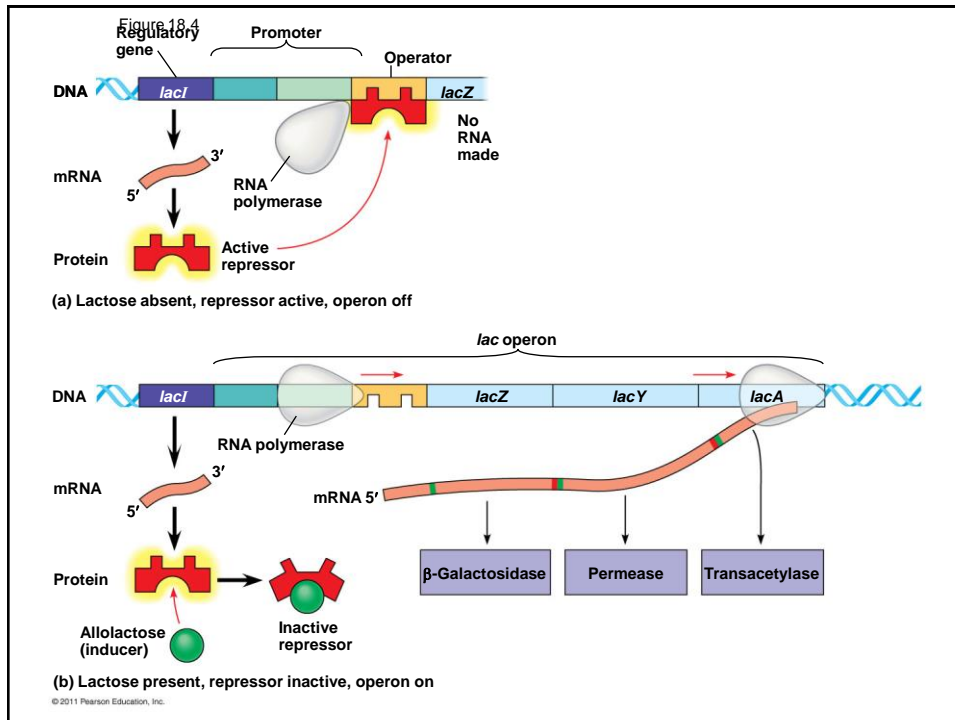
Repressible and Inducible Operons: Two Types of Negative Gene Regulation

- A repressible operon is one that is usually on; binding of a repressor to the operator shuts off transcription
- The *trp* operon is a repressible operon
- An inducible operon is one that is usually off; a molecule called an inducer inactivates the repressor and turns on transcription

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- The *lac* operon is an inducible operon and contains genes that code for enzymes used in the metabolism of lactose
- By itself, the *lac* repressor is active and switches the *lac* operon off
- A molecule called an **inducer** inactivates the repressor to turn the *lac* operon on

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- Regulation of the *trp* and *lac* operons involves **NEGATIVE** control of genes because **operons are switched off** by the **active form of the repressor**.

Positive Gene Regulation

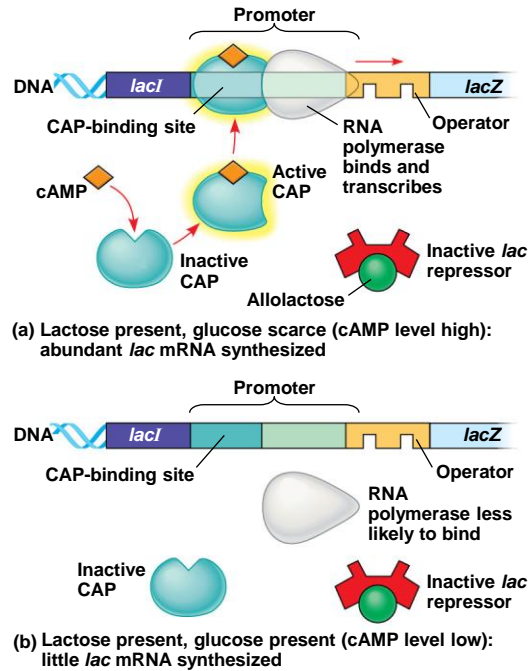
- Some operons are also subject to positive control through a stimulatory protein, such as catabolite activator protein (CAP), an **activator** of transcription
- When glucose (preferred by *E. coli*) is scarce, CAP is activated by binding with **cyclic AMP (cAMP)**
- Activated CAP attaches to the promoter of the *lac* operon and increases the affinity of RNA polymerase, thus accelerating transcription

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- When glucose levels increase, CAP detaches from the *lac* operon, and transcription returns to a normal rate
- CAP helps regulate other operons that encode enzymes used in catabolic pathways

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Figure 18.5



Concept 18.2: Eukaryotic gene expression is regulated at many stages

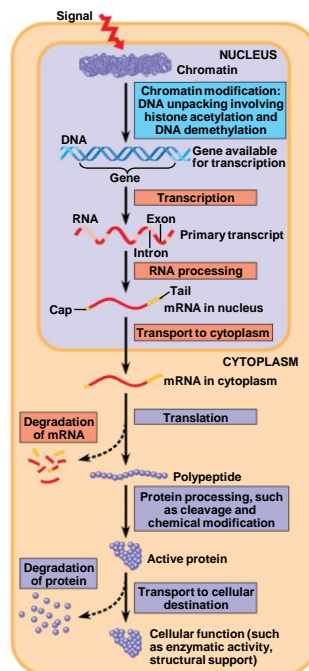
- All organisms must regulate which genes are expressed at any given time
- In multicellular organisms regulation of gene expression is essential for cell specialization

Differential Gene Expression

- Almost all the cells in an organism are genetically identical
- Differences between cell types result from **differential gene expression**, the expression of different genes by cells with the same genome
- Abnormalities in gene expression can lead to diseases including cancer
- Gene expression is regulated at many stages

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Figure 18.6



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Regulation of Chromatin Structure

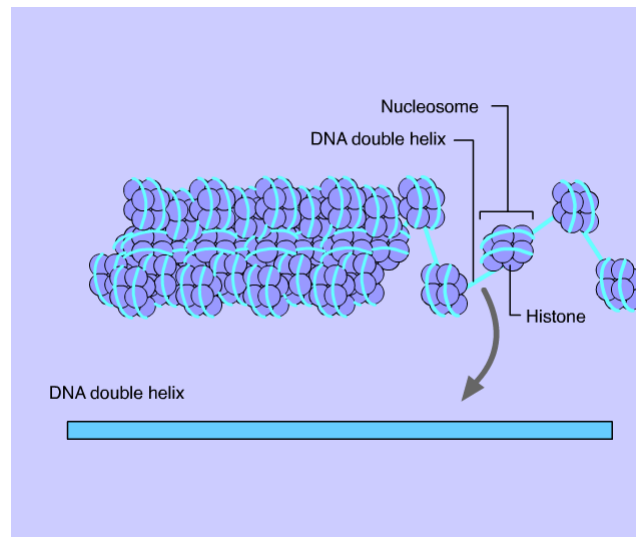
- Genes within highly packed heterochromatin are usually not expressed
- Chemical modifications to histones and DNA of chromatin influence both chromatin structure and gene expression

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Histone Modifications

- In **histone acetylation**, acetyl groups are attached to positively charged lysines in histone tails
- This loosens chromatin structure, thereby promoting the initiation of transcription
- The addition of methyl groups (methylation) can condense chromatin; the addition of phosphate groups (phosphorylation) next to a methylated amino acid can loosen chromatin

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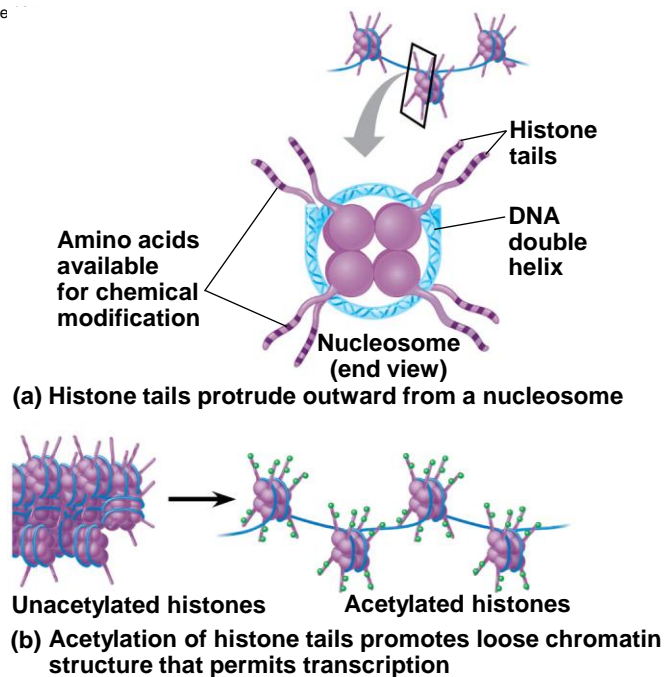


Animation: DNA Packing

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Figure 17-17



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DNA Methylation

- **DNA methylation**, the addition of methyl groups to certain bases in DNA, is associated with reduced transcription in some species
- DNA methylation can cause long-term inactivation of genes in cellular differentiation

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Epigenetic Inheritance

- Although the chromatin modifications just discussed do not alter DNA sequence, they may be passed to future generations of cells
- The inheritance of traits transmitted by mechanisms not directly involving the nucleotide sequence is called **epigenetic inheritance**

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Regulation of Transcription Initiation

- Chromatin-modifying enzymes provide initial control of gene expression by making a region of DNA either more or less able to bind the transcription machinery

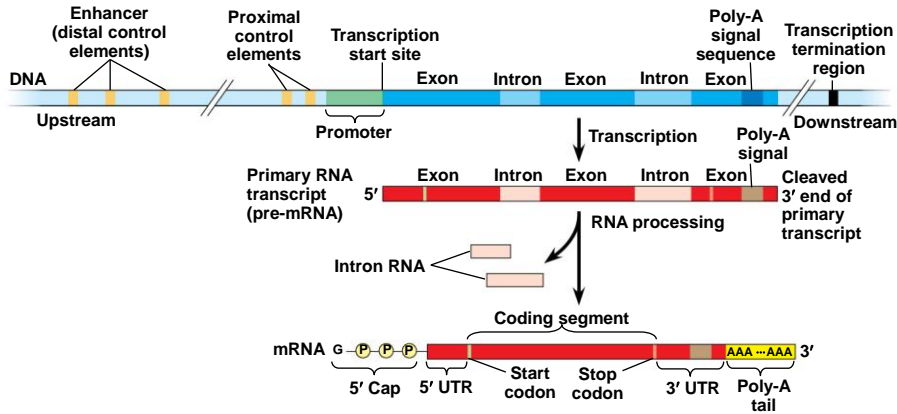
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Organization of a Typical Eukaryotic Gene

- Associated with most eukaryotic genes are multiple **control elements**, segments of noncoding DNA that serve as binding sites for transcription factors that help regulate transcription
- Control elements and the transcription factors they bind are critical to the precise regulation of gene expression in different cell types

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Figure 18.8-3



The Roles of Transcription Factors

- To initiate transcription, eukaryotic RNA polymerase requires the assistance of proteins called transcription factors
- General transcription factors are essential for the transcription of all protein-coding genes
- In eukaryotes, high levels of transcription of particular genes depend on control elements interacting with specific transcription factors

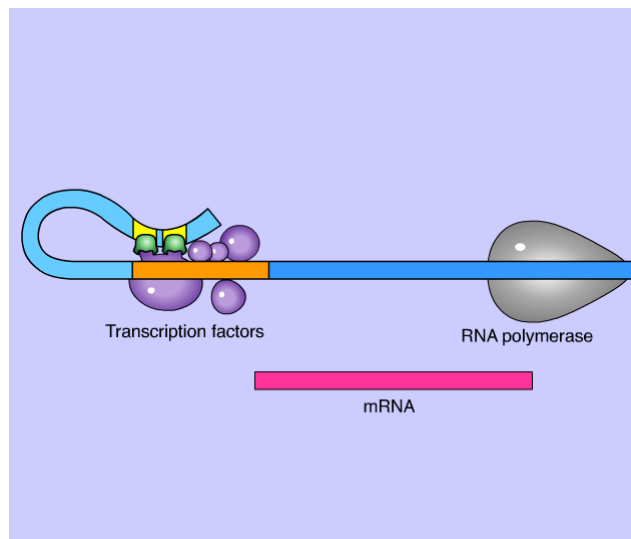
Enhancers and Specific Transcription Factors

- Proximal control elements are located close to the promoter
- Distal control elements, groupings of which are called **enhancers**, may be far away from a gene or even located in an intron

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- An activator is a protein that binds to an enhancer and stimulates transcription of a gene
- Activators have two domains, one that binds DNA and a second that activates transcription
- Bound activators facilitate a sequence of protein-protein interactions that result in transcription of a given gene

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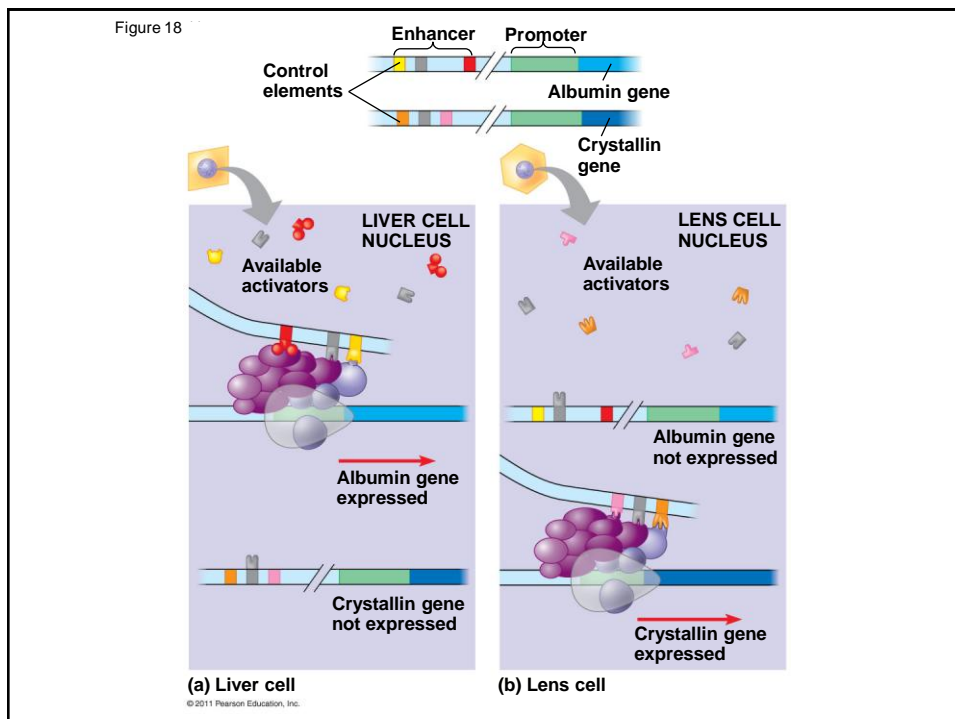
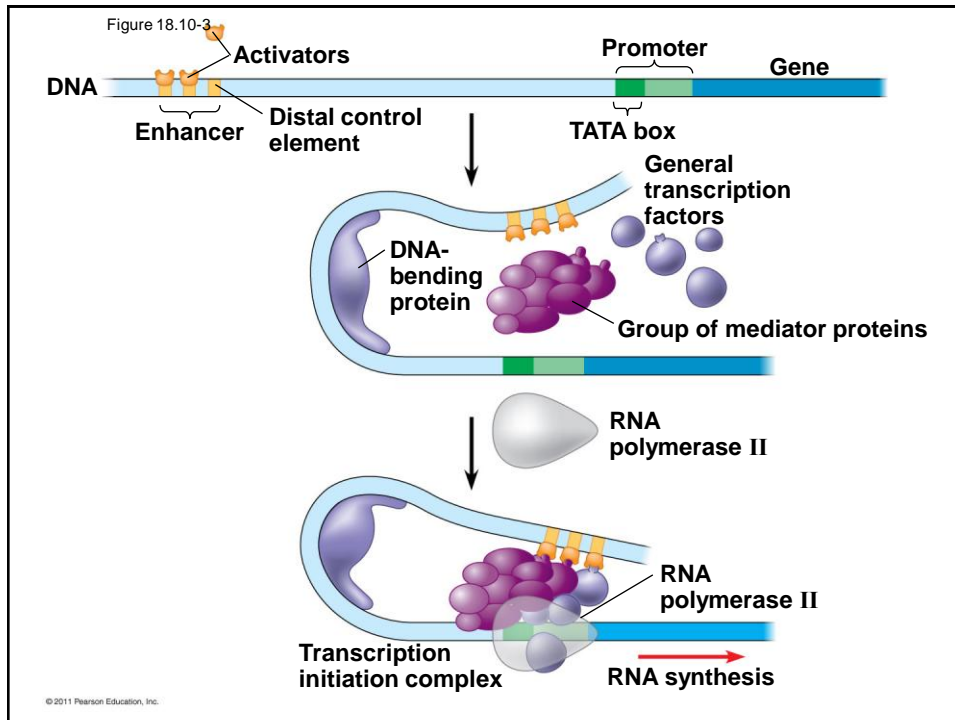


Animation: Initiation of Transcription
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- Some transcription factors function as repressors, inhibiting expression of a particular gene by a variety of methods
- Some activators and repressors act indirectly by influencing chromatin structure to promote or silence transcription

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Coordinately Controlled Genes in Eukaryotes

- Unlike the genes of a prokaryotic operon, **each** of the co-expressed eukaryotic genes has a promoter and control elements
- These genes can be scattered over different chromosomes, but each has the same combination of control elements
- Copies of the activators recognize specific control elements and promote simultaneous transcription of the genes

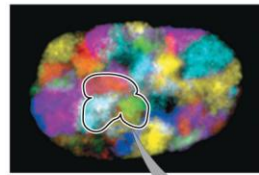
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Nuclear Architecture and Gene Expression

- Loops of chromatin extend from individual chromosomes into specific sites in the nucleus
- Loops from different chromosomes may congregated at particular sites, some of which are rich in transcription factors and RNA polymerases
- These may be areas specialized for a common function

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Figure 18.12

Chromosomes in the interphase nucleus10 μm **Chromosome territory****Chromatin loop****Transcription factory**

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Mechanisms of Post-Transcriptional Regulation

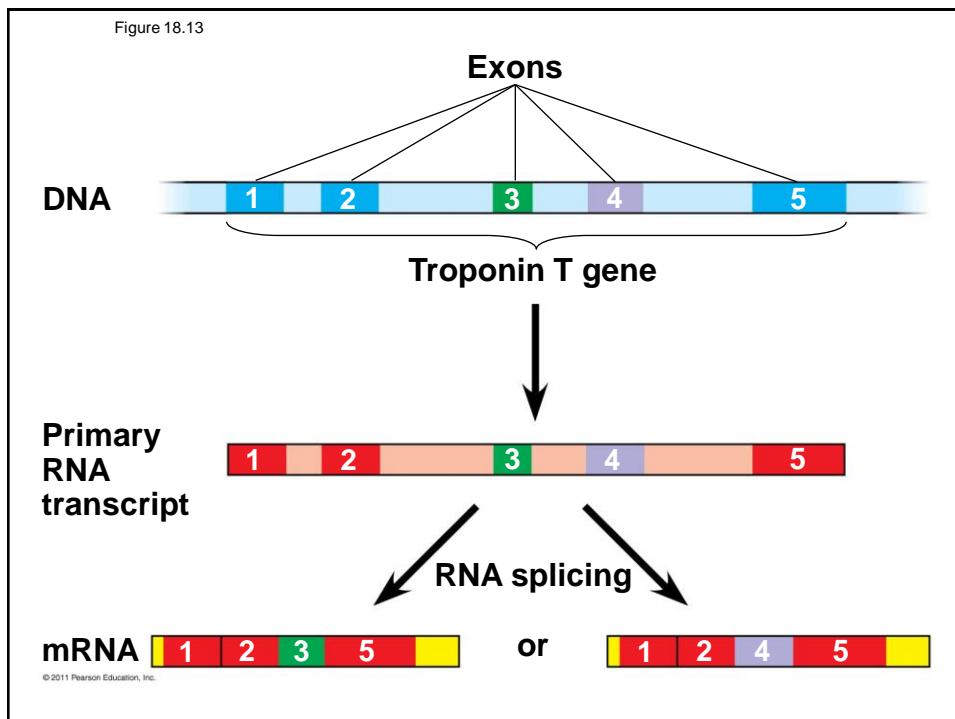
- Transcription alone does not account for gene expression
- Regulatory mechanisms can operate at various stages after transcription
- Such mechanisms allow a cell to fine-tune gene expression rapidly in response to environmental changes

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RNA Processing

- In **alternative RNA splicing**, different mRNA molecules are produced from the same primary transcript, depending on which RNA segments are treated as exons and which as introns

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mRNA Degradation

- The life span of mRNA molecules in the cytoplasm is a key to determining protein synthesis
- Eukaryotic mRNA is more long lived than prokaryotic mRNA
- Nucleotide sequences that influence the lifespan of mRNA in eukaryotes reside in the untranslated region (UTR) at the 3' end of the molecule

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Longer-lived mRNA



Animation: mRNA Degradation

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Initiation of Translation

- The initiation of translation of selected mRNAs can be blocked by regulatory proteins that bind to sequences or structures of the mRNA
- Alternatively, translation of all mRNAs in a cell may be regulated simultaneously
- For example, translation initiation factors are simultaneously activated in an egg following fertilization

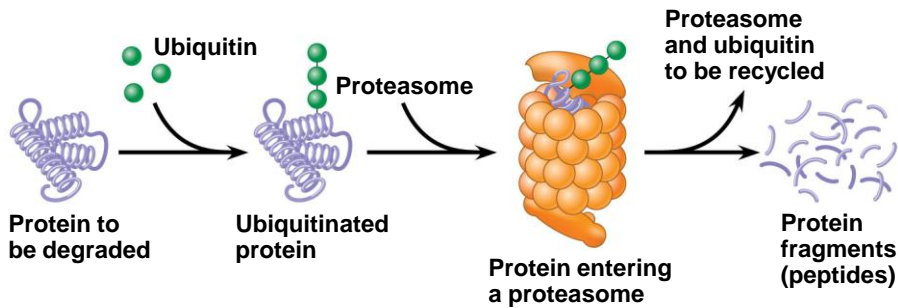
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Protein Processing and Degradation

- After translation, various types of protein processing, including cleavage and the addition of chemical groups, are subject to control
- **Proteasomes** are giant protein complexes that bind protein molecules and degrade them

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Figure 18.14



Concept 18.3: Noncoding RNAs play multiple roles in controlling gene expression

- Only a small fraction of DNA codes for proteins, and a very small fraction of the non-protein-coding DNA consists of genes for RNA such as rRNA and tRNA
- A significant amount of the genome may be transcribed into noncoding RNAs (ncRNAs)
- Noncoding RNAs regulate gene expression at two points: mRNA translation and chromatin configuration

Effects on mRNAs by MicroRNAs and Small Interfering RNAs

- **MicroRNAs (miRNAs)** are small single-stranded RNA molecules that can bind to mRNA
- These can degrade mRNA or block its translation

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- The phenomenon of inhibition of gene expression by RNA molecules is called **RNA interference (RNAi)**
- RNAi is caused by **small interfering RNAs (siRNAs)**
- siRNAs and miRNAs are similar but form from different RNA precursors

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The Evolutionary Significance of Small ncRNAs

- Small ncRNAs can regulate gene expression at multiple steps
- An increase in the number of miRNAs in a species may have allowed morphological complexity to increase over evolutionary time

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Concept 18.4: A program of differential gene expression leads to the different cell types in a multicellular organism

- During embryonic development, a fertilized egg gives rise to many different cell types
- Cell types are organized successively into tissues, organs, organ systems, and the whole organism
- Gene expression orchestrates the developmental programs of animals

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A Genetic Program for Embryonic Development

- The transformation from zygote to adult results from cell division, cell differentiation, and morphogenesis

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- **Cell differentiation** is the process by which cells become specialized in structure and function
- The physical processes that give an organism its shape constitute **morphogenesis**
- Differential gene expression results from genes being regulated differently in each cell type
- Materials in the egg can set up gene regulation that is carried out as cells divide

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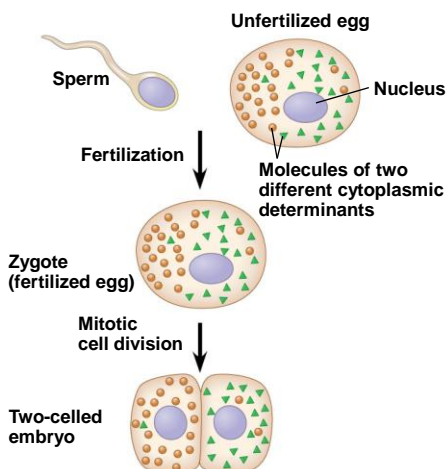
Cytoplasmic Determinants and Inductive Signals

- An egg's cytoplasm contains RNA, proteins, and other substances that are distributed unevenly in the unfertilized egg
- **Cytoplasmic determinants** are maternal substances in the egg that influence early development
- As the zygote divides by mitosis, cells contain different cytoplasmic determinants, which lead to different gene expression

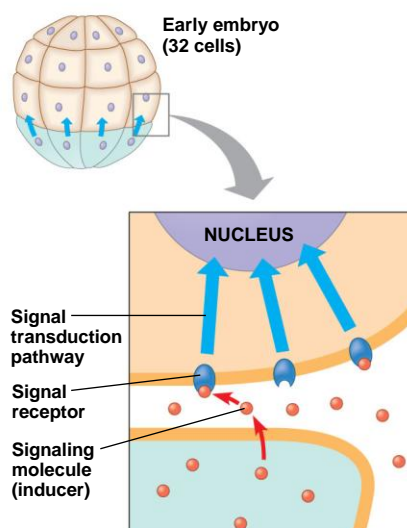
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Figure 18.17

(a) Cytoplasmic determinants in the egg



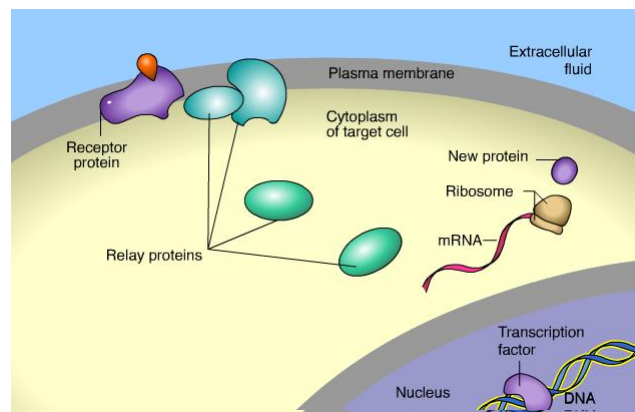
(b) Induction by nearby cells



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- The other important source of developmental information is the environment around the cell, especially signals from nearby embryonic cells
- In the process called **induction**, signal molecules from embryonic cells cause transcriptional changes in nearby target cells
- Thus, interactions between cells induce differentiation of specialized cell types

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Animation: Cell Signaling

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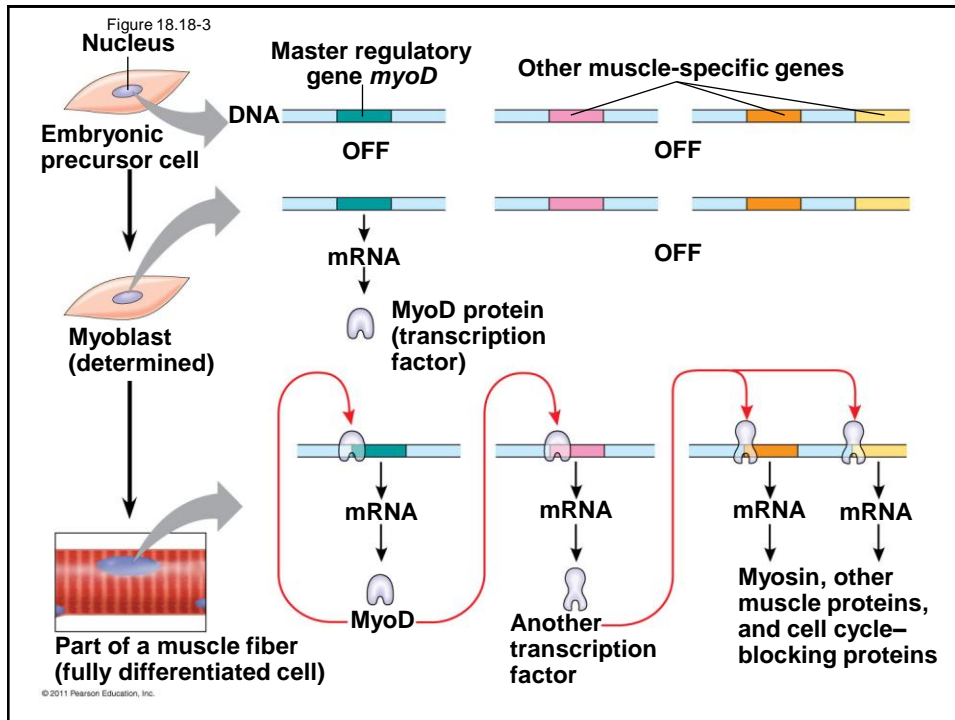
Sequential Regulation of Gene Expression During Cellular Differentiation

- **Determination** commits a cell to its final fate
- Determination precedes differentiation
- Cell differentiation is marked by the production of tissue-specific proteins

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- Myoblasts produce muscle-specific proteins and form skeletal muscle cells
- *MyoD* is one of several “master regulatory genes” that produce proteins that commit the cell to becoming skeletal muscle
- The MyoD protein is a transcription factor that binds to enhancers of various target genes

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Pattern Formation: Setting Up the Body Plan

- **Pattern formation** is the development of a spatial organization of tissues and organs
- In animals, pattern formation begins with the establishment of the major axes
- **Positional information**, the molecular cues that control pattern formation, tells a cell its location relative to the body axes and to neighboring cells

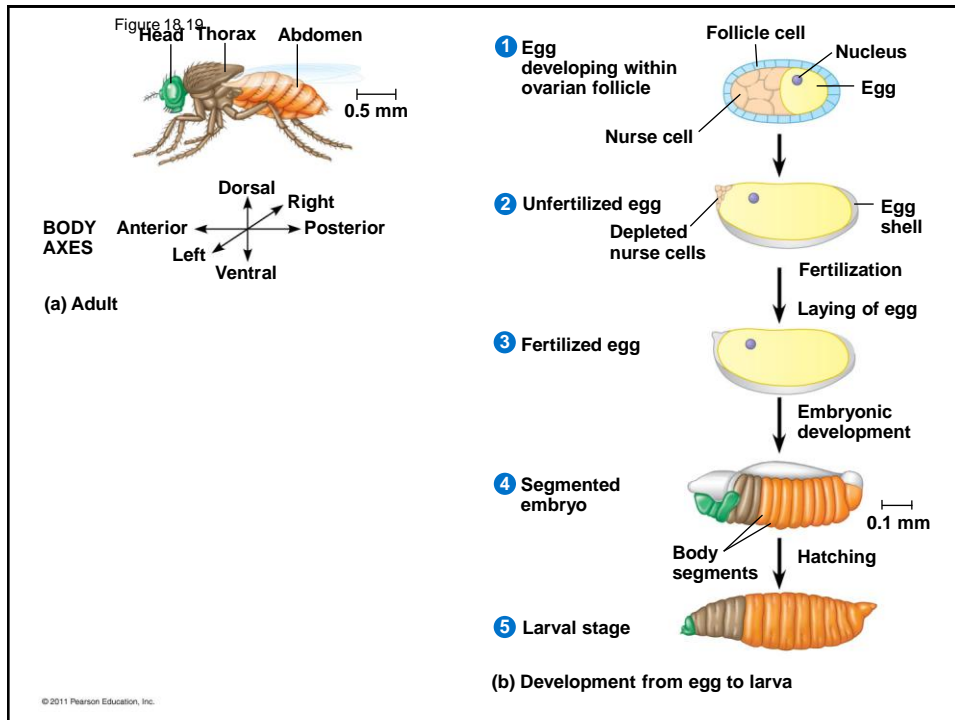
- Pattern formation has been extensively studied in the fruit fly *Drosophila melanogaster*
- Combining anatomical, genetic, and biochemical approaches, researchers have discovered developmental principles common to many other species, including humans

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The Life Cycle of Drosophila

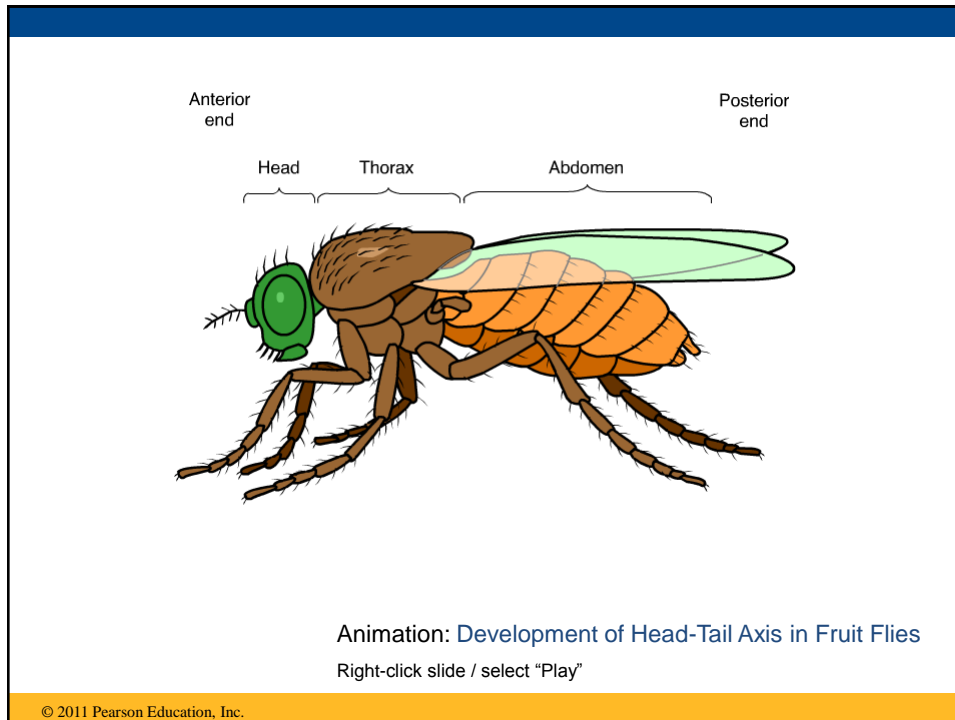
- In *Drosophila*, cytoplasmic determinants in the unfertilized egg determine the axes before fertilization
- After fertilization, the embryo develops into a segmented larva with three larval stages

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Axis Establishment

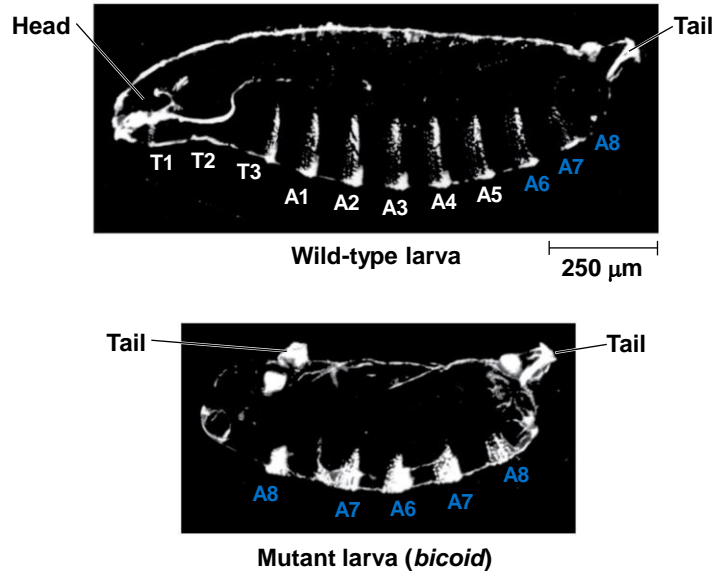
- **Maternal effect genes** encode for cytoplasmic determinants that initially establish the axes of the body of *Drosophila*
- These maternal effect genes are also called **egg-polarity genes** because they control orientation of the egg and consequently the fly



Bicoid: A Morphogen Determining Head Structures

- One maternal effect gene, the *bicoid* gene, affects the front half of the body
- An embryo whose mother has no functional *bicoid* gene lacks the front half of its body and has duplicate posterior structures at both ends

Figure 18.21



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- This phenotype suggests that the product of the mother's *bicoid* gene is concentrated at the future anterior end
- This hypothesis is an example of the morphogen gradient hypothesis, in which gradients of substances called **morphogens** establish an embryo's axes and other features

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Figure 18.UN04a

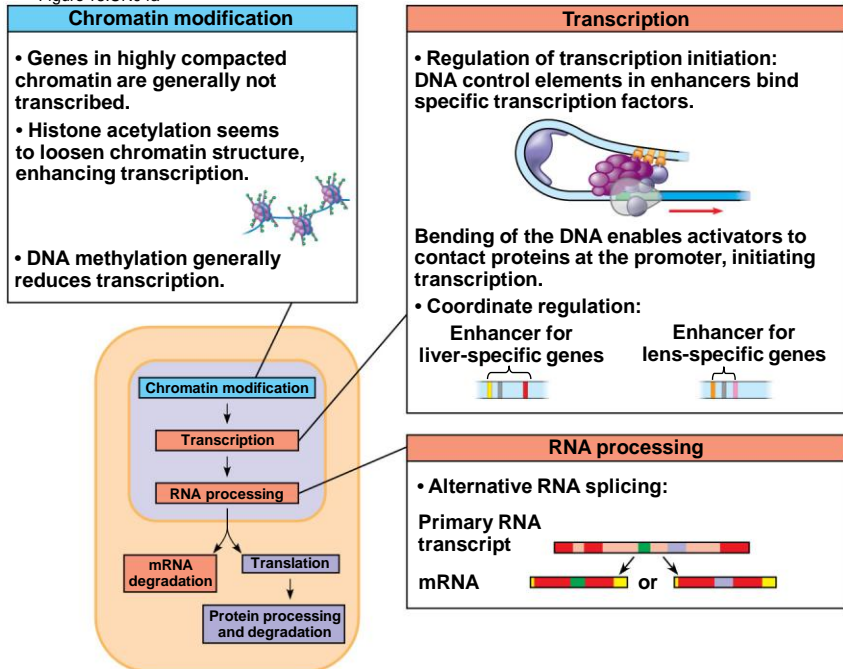


Figure 18.UN04b

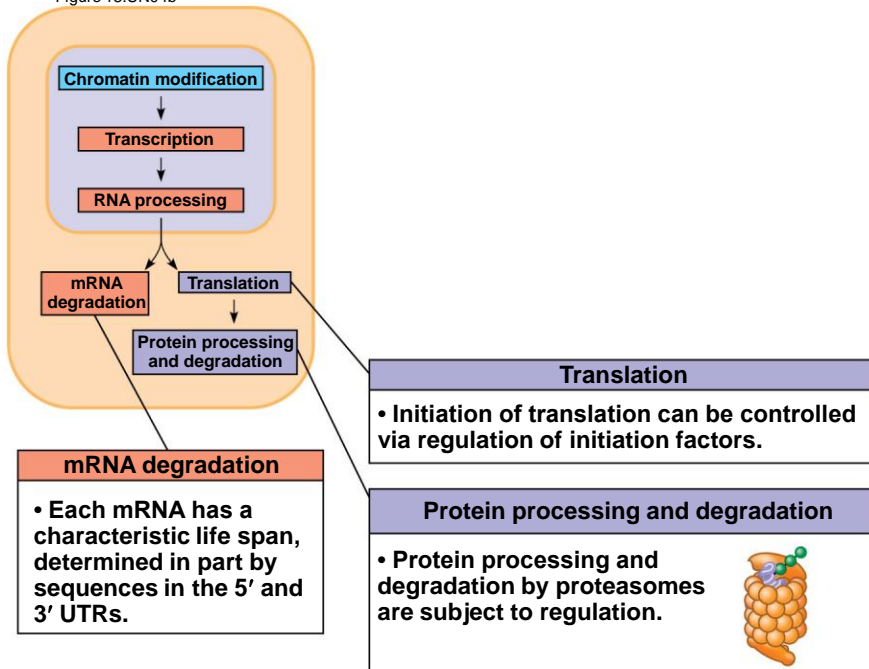


Figure 18.UN05

